Appl. No. 09/825,242
Amdt. dated December 4, 2003
Reply to Office Action of September 24, 2003

PATENT

REMARKS/ARGUMENTS

Claims 35 and 37-43, 48, 49 and 52 are pending and have been examined. Claim 53 is added. Claim 35 has been amended to incorporate the additional step of previous claim 36, which has been cancelled. New claim 53 is the same as old claim 35 except that the preamble has been amended to recite "designing" instead of producing and to recite that the method is "computer-implemented" (see paragraph 138 et seq. of published version of application.) Applicants respond to the Examiner's comments using the paragraph numbering of the office action.

1-2.   Rejection under 35 USC 112, second paragraph

Claims 35, 40-43 and 52 stand rejected as missing an essential step. The Examiner suggests amending the preamble to recite a method of designing a zinc finger protein. However, applicants have amended the claims to include an additional step of producing a protein. This step is consistent with the preamble. New claim 53 has been added based on old claim 53. New claim 53 does recite "designing" in the preamble consistent with the Examiner's suggestion.

Claim 43 is said to lack antecedent basis for the "third triplet in the target site" recited in line 14 and lines 17-18. However, antecedent basis is provided in step (b) of the claim referring to a "target site comprising contiguous first, second and third triplets."

3-4.   Claims 35-40, 42 and 43 stand rejected under 35 USC 102(b) as anticipated by Desjarlais. The Examiner says the claims are drawn to method of designing and synthesizing a zinc finger protein comprising three zinc fingers by using a database that comprises a plurality of zinc finger protein sequences in which the zinc finger domains are correlated with their respective target sequences. The Examiner says Desjarlais shows a database in Figure 1 comprising two zinc finger proteins and their targets, and that Desjarlais shows binding of the zinc finger proteins to their target in Figs. 3 and 4. This rejection is respectfully traversed.

Initially, it is noted that the Examiner's statement of what is being claimed is an oversimplification. The claims do not merely recite using a database to design a zinc finger protein, but rather recite several distinct steps by which this process is accomplished. The

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process starts with a database storing information regarding the amino acid sequences of fingers from zinc finger proteins and their corresponding nucleotide target sequences. A target site is then provided for design of a zinc finger protein. The method searches through the database to find zinc finger proteins, each of which comprises a finger that bind to at least one triplet of the targets, organizing such zinc finger proteins in subsets according to which triplet they bind, and then outputting the subsets. Component fingers from the zinc finger proteins in the various subsets can then be combined to form a novel zinc finger protein that binds to the target site. Optionally, the methods identify subsets of zinc finger proteins comprising a finger that specifically binds to a triplet at a particular triplet position within the target site from the corresponding finger position in a known protein in the database (see e.g., claim 37). The zinc fingers in such subsets are particularly advantageous for design because they are more likely to bind with the same specificity and affinity in a novel zinc finger protein as they do in the known zinc finger protein in the database. The Examiner is referred to the detailed description of the claimed methods at paragraphs 0110 to 0118 of the published version of the application.

The cited reference merely provides a tabulation of two zinc finger proteins and their respective target sequences and shows that the zinc finger proteins bind to their target sequence. Even if it is assumed *arguendo* that a tabulation of two zinc finger proteins and their respective target sequences is considered to be a database, as recited in step (a) of claim 35, the cited reference does not disclose any of the other steps (b), (c) and (d) in claim 35. For example, if the two target sites in Fig. 1 of Desjarlais are considered to fulfill the requirement of step (a) (providing a database), they cannot also fulfill the requirement of step (b) (providing a target sequence for design of a zinc finger protein). Desjarlais also provides no disclosure of identifying first, second and third sets of zinc finger proteins in the database as recited in step (c) of claim 35. Perforce, Desjarlais does not disclose outputting designations and subdesignations of the zinc finger proteins in the first, second and third sets, as recited in step (d) of claim 35. The same distinctions apply *mutatis mutandis* to independent claims 42 and 43. For these reasons, withdrawal of the rejection is respectfully requested.

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7-8. Claims 48 and 49 stand rejected as obvious under 35 USC 103(a) over Desjarlais. Desjarlais is applied as above. The Examiner takes the view that it would have been obvious to automate the procedure of Desjarlais using a computer to assemble and utilize the database on the basis that automation is an obvious process (citing to MPEP 2144.014). This rejection is respectfully traversed.

Claims 48 and 49 are distinguished over Desjarlais for analogous reasons to claim 35. No secondary reference has been cited to compensate for these deficiencies. In addition, it was not obvious to use a computer to automate Desjarlais method because Desjarlais does not disclose any discrete steps in forming or using a database that would be amenable to computerized automation. As noted above, Desjarlais merely tabulates two zinc finger proteins and their target sequences, and then shows binding of the zinc finger proteins to their target sequences. It is not apparent what role computer automation would have in this process. For this reason as well as those discussed in connection with claim 35, withdrawal of the rejection is respectfully traversed.

9-10. Claim 41 stands rejected as obvious over claim 1 of US 6,453,242. The Examiner says that although the conflicting claims are not identical, the differences are minor in nature. This rejection is respectfully traversed. A double patenting rejection of the obviousness types is analogous to the nonobviousness requirement of 35 USC 103, except that the patent principally underlying the double patenting rejection is not considered prior art. *In re Braithwaite,* 154 USPQ 29 (CCPA 1967). A double patenting rejection should therefore make clear the differences between the inventions defined by the conflicting claims and the reasons why a person of ordinary skill in the art would conclude that the invention defined in the claim in issue is an obvious variation of the invention defined in a claim in the patent. MPEP 804B. 1. Here, the claims of the '242 patent do not disclose any of the steps recited in claim 35. Claim 41 includes all of these steps by its dependency from claim 35. The office action does not cite a secondary reference to combine with the claims of the primary reference with respect to these claim elements or point to any motivation to modify the teaching of the claims of the '242 patent. Accordingly, it is submitted that a prima facie case has not been established.

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Further, it is noted that the claims in the '242 patent were divided from the remaining claims of 09/229,007 (which gave rise to US 6,453,242) by restriction requirement in an office action dated March 12, 2001. At the time of the restriction requirement, the pending claims included both claims of the type that issued as '242 and of the type now pending. Thus, the restriction requirement concluded that the claims of the '242 patent are patentably distinct from those pending in the present application. Thus, restriction is precluded under 35 USC 121.

11. Claims 35, 41, 48, 49 and 52 stand rejected as provisionally obvious over claims 22, 32, 44, 46 of USSN 10/113,424. The Examiner says that although the conflicting claims are not identical, they are not patentably distinct from each other because the copending claims are species of present claims 35, 41, 48, 49 and 52 and the differences are minor. This rejection is respectfully traversed for essentially the same reasons as in 9-10 above.

First, steps (a)-(d) of claims 35 and 48 and elements (1)-(4) of claim 49 are not disclosed by any of the claims in the '424 application. Present claims 41 and 52 depend from claim 35 and include the same elements. The claims of the '424 application are not species of the present claims because they lack several of the element in the present claims. The office action has not cited any secondary reference to combine with the '424 claims nor pointed to any motivation to support the combination. Accordingly, it is submitted that a prima facie case of double patenting has not been established.

Second, it is noted that the claims in the present case were divided from the remaining claims of parent case 09/229,007 (which gave rise to US 6,453,242) by restriction requirement in an office action dated March 12, 2001. At the time of the restriction requirement, the pending claims included claims of the type that issued as '242, those in the '424 application, and of the type now pending here. The restriction requirement concluded that claims of the type now pending here were patentably distinct from claims of the type now pending in the '424 application.
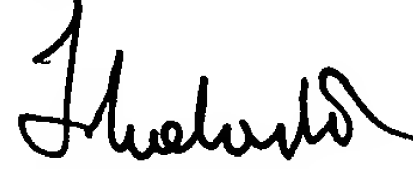
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If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,

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Attachments
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